(a) contacting said surface with a first protected amino acid wherein said first protected amino acid is selectively coupled to a functional group in a first selectively activated region of said surface;

(b) contacting said surface with a second protected amino acid wherein said second protected amino acid is selectively coupled to a functional group in a second selectively activated region of said surface; and,

(c) repeating the above steps until at least two different polypeptides are formed at known locations on said substrate surface.

173. (New) The method as recited in claim **172**, wherein contacting said surface with said second protected amino acid is accomplished without physical segregation of said surface.

174. (New) The method as recited in claim **172**, wherein said at least two different polypeptides each occupy an area on said substrate of less than about 1 cm^2 to about $1x10^{-5}$ cm^2.

175. (New) The method as recited in claim **174**, wherein said at least two different polypeptides each occupy an area on said substrate of less than about $1x10^{-1}$ cm^2 to about $1x10^{-4}$ cm^2.

176. (New) The method as recited in claim **175**, wherein said at least two different polypeptides each occupy an area on said substrate of less than about $1x10^{-2}$ cm^2 to about $1x10^{-3}$ cm^2.

177. (New) The method as recited in claim **172**, repeating said steps above until said at least two different polypeptides exceed a density of about 400 different polypeptides /cm^2.

178. (New) The method as recited in claim **172**, repeating said steps above until said at least two different polypeptides exceed a density of about 1000 different polypeptides /cm^2.

179. (New) The method as recited in claim **172**, wherein said method produces a substrate that contains more than 100 different polypeptides per cm^2.

180. (New) The method as recited in claim **172**,wherein said method produces a substrate that contains more than 1,000 different polypeptides per cm^2.

181. (New) The method as recited in claim **172**, wherein said method produces a substrate that contains more than 10,000 different polypeptides per cm^2.

182. (New) The method as recited in claim **172**, wherein said method produces a substrate that contains more than 100,000 different polypeptides per cm^2.

Sub A7 **183**. (New) A method for synthesizing polypeptides on a substrate, said method comprising:

a) providing a substrate wherein said substrate comprises immobilized polypeptide molecules, said polypeptide molecules coupled to a removable protecting groups;

b) removing said protecting group from said polypeptide molecules in a first predefined region of said substrate without removing said protecting groups from a second predefined region of said substrate; and

c) contacting said substrate with a first amino acid to couple said first amino acid to said polypeptide molecules in said first predefined region, said first amino acid having a amino acid protecting group thereon, forming a first polypeptide on said substrate in said first predefined region that is different from an polypeptide in said second predefined region.

184. (New) The method as recited in claim **183**, wherein said step of removing is an irradiation step.

Sub D5 **185**. (New) The method as recited in claim **184**, wherein said step of irradiating is a step of masking a light source with a mask placed between said light source and said substrate, said mask comprising first transparent regions and second opaque regions,

said transparent regions transmitting light from said source to at least said first predefined region, and said opaque regions blocking light from said source to at least said second predefined region.

186. (New) The method as recited in claim **183**, wherein said first and second regions each have total areas less than about 1 cm^2.

187. (New) The method as recited in claim **184**, wherein said steps of irradiating are conducted with a monochromatic light.

188. (New) The method as recited in claim **184**, wherein said steps of irradiating and contacting are repeated so as to synthesize 10^3 different polypeptides on said substrate.

189. (New) The method as recited in claim **184**, wherein the step of irradiating a first predefined region is a step of irradiating half of a region of said substrate irradiated in a prior synthesis step, and not irradiating half of said region irradiated in a prior synthesis step.

190. (New) The method as recited in claim **183**, wherein said steps a) and b) are repeated to synthesize more than 1,000 different polypeptides on different synthesis regions of said substrate, each of said different polypeptides occupying an area of less than about 10^{-2} cm^2 to about $1x10^{-5}$ cm^2.

191. (New) The method as recited in claim **190**, wherein said steps a) and b) are repeated to synthesize more than 1,000 different polypeptides on different synthesis regions of said substrate, each of said different polypeptides occupying an area of less than about 10^{-2} cm^2 to about $1x10^{-4}$ cm^2.

192. (New) The method as recited in claim **191**, wherein said steps a) and b) are repeated to synthesize more than 1,000 different polypeptides on different synthesis

regions of said substrate, each of said different polypeptides occupying an area of less than about 10^{-2} cm^2 to about $1x10^{-3}$ cm^2.

SUB D5 CONT.

193. (New) A method of synthesizing polypeptides, said method comprising:

a) generating a pattern of light and dark areas by selectively irradiating at least a first area of a surface of a substrate, said surface comprising immobilized amino acids on said surface, said amino acids coupled to a photoremovable protective group, without irradiating at least a second area of said surface, to remove said protective group from said amino acids in said first area;

b) simultaneously contacting said first area and said second area of said surface with a first amino acid to couple said first amino acid to said immobilized amino acids in said first area, and not in said second area, said first amino acid having said photoremovable protective group;

c) generating another pattern of light and dark areas by selectively irradiating with light at least a part of said first area of said surface and at least a part of said second area to remove said protective group in said at least a part of said first area and said at least a part of said second area;

d) simultaneously contacting said first area and said second area of said surface with a second amino acid to couple said second amino acid to said immobilized amino acids in at least a part of said first area and at least a part of said second area; and

e) performing additional irradiating and amino acid contacting and coupling steps so that a matrix array of at least 100 different polypeptides is formed on said surface, each different polypeptide synthesized in an area of less than 0.1 cm^2, whereby said different polypeptides have sequences and locations on said surface defined by the patterns of light and dark areas formed during the irradiating steps and the amino acids coupled in said contacting steps.

194. (New) The method as recited in claim **193**, wherein said substrate is selected from the group consisting of Langmuir Blodgett film, glass, germanium, silicon,

(poly)tetrafluorethylene, polystyrene, gallium arsenide, gallium phosphide, silicon oxide, silicon nitride, and combinations thereof.

Sub D6

195. (New) The method as recited in claim **193**, wherein said protective group is selected from the group consisting of 6-nitroveratryloxycarbonyl, 2-nitrobenzyloxy carbonyl, dimethyl dimethoxybenzyloxy carbonyl, 5-bromo-7-nitroindolinyl, o-hydroxyalpha-methyl cinnamoyl, 2-oxymethylene anthriquinone, and mixtures thereof.

196. (New) The method as recited in claim **193**, wherein each different polypeptide synthesized is in an area of less than about 0.1 cm^2 to about $1x10^{-5}$ cm^2.

197. (New) The method as recited in claim **196**, wherein each different polypeptide synthesized is in an area of less than about $1x10^{-1}$ cm^2 to about $1x10^{-4}$ cm^2.

198. (New) The method as recited in claim **197**, wherein each different polypeptide synthesized is in an area of less than about $1x10^{-2}$ cm^2 to about $1x10^{-3}$ cm^2.

199. (New) The method as recited in claim **193**, wherein said matrix array is at least 400 different polypeptides/ cm^2.

200. (New) The method as recited in claim **193**, wherein said matrix array is at least 1000 different polypeptides /cm^2.

201. (New) The method as recited in claim **193**, wherein said method produces a substrate that contains more than 1,000 different polypeptides per 0.1 cm^2.

202. (New) The method as recited in claim **193**, wherein said method produces a substrate that contains more than 10,000 different polypeptides per 0.1 cm^2.

203. (New) The method as recited in claim **193**, wherein said method produces a substrate that contains more than 100,000 different polypeptides per 0.1 cm^2.

204. (New) The method as recited in claim **193**, wherein the irradiating step c) further comprises:

i) placing a mask adjacent to said substrate, said mask having substantially transparent regions and substantially opaque regions at a wavelength of light; and

ii) illuminating said mask with a light source, said light source producing at least said wavelength of light, said mask permitting illumination of half of said substrate which was illuminated and half of said substrate which was not illuminated in said step a).

205. (New) The method as recited in claim **204**, wherein said additional steps are performed so as to synthesize 10^3 different polypeptides in 10^3 respective preselected regions on said substrate.

206. (New) The method as recited in claim **204**, wherein said additional steps are performed so as to synthesize 10^6 different polypeptides in 10^6 respective preselected regions on said substrate.

207. (New) The method of claim **204**, wherein said additional steps are performed so that at least 1,000 different polypeptides are synthesized on said surface, and each different polypeptide is contained within an area less than about 1×10^{-3} cm^2.

208. (New) The method of claim **193**, wherein said immobilized amino acids are attached to said surface by a linker selected from the group consisting of aryl acetylene and ethylene glycol.

209. (New) The method of claim **193**, wherein said immobilized amino acids are attached to said surface by polyethylene glycol.

REMARKS

Claims 172-209 are pending in this application and presented for examination. Claims 1-171 have been canceled without prejudice or disclaimer. Early examination on the merits is respectfully requested.

THE APPLICATION